

## APPENDIX E

### Specification Support for Constructive Reduction within the Scope of Count 1

<u>Representative Claim</u>	<u>Support in Specification</u>
<p><b>Claim 1795.</b>  A process for determining the sequence of a nucleic acid of interest comprising:</p> <p>providing or generating detectable non-radioactively labeled nucleic acid fragments comprising: (a) a sequence complementary to said nucleic acid of interest or a portion thereof, and (b) fluorescent labels covalently attached, directly or through a linkage group, to said fragments;</p> <p>subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments;</p>	<p>Support for a method of determining the sequence of a nucleic acid of interest can be found, for instance, on page 84, 2<sup>nd</sup> ¶, which states that the signaling molecules of the invention are “particularly important for detecting nucleic acids in gels (for example, sequencing gels).”</p> <p>The specification provides support for detectable nucleic acid fragments labeled by one or more non-radioactive indicator molecules, <i>e.g.</i>, fluorescent dyes, including fluorescein, rhodamine and dansyl. <i>See, e.g.</i>, page 26, 1<sup>st</sup> ¶; example 9 on pages 46 through 47; page 96, last ¶ through page 97 1<sup>st</sup> ¶, and original Claims 42, 43, 88, 89, and 130-133. The specification discloses that the DNA and RNA probes comprise a nucleotide sequence substantially matching the nucleic acid sequence of interest and upon localization of the probe to the nucleic acid sequence of interest the resulting hybrid can be observed and identified. <i>See, e.g.</i>, page 98, final ¶ through page 100, 1<sup>st</sup> ¶. The specification also provides specific support for attachment of fluorescent indicator molecules “directly or through a chemical linkage or linker arm to the nucleotide” on page 96, last paragraph to page 97 1<sup>st</sup> full paragraph. <i>See also, e.g.</i>, page 95, 1<sup>st</sup> ¶; and page 96, 1<sup>st</sup> ¶ (“The nucleotides are then modified...by having covalently attached thereto, to the P moiety and/or the S moiety and/or the B moiety, a chemical moiety Sig.”).</p> <p>Separating and resolving are disclosed throughout the specification. For instance, the term “resolving” or “resolution” appear on pages 31 (1<sup>st</sup> full ¶) and 33 (1<sup>st</sup> full ¶). Furthermore, the specification provides support for “sequencing gel,” <i>e.g.</i>, page 84, which necessarily involves separating and resolving nucleic acid fragments.</p>

<u>Representative Claim</u>	<u>Support in Specification</u>
detecting non-radioactively said separated or resolved fragments by means of said attached fluorescent labels; and	Detecting the presence of the fragments is disclosed throughout the entire specification, such as in the Abstract, page 6 (penultimate ¶), page 84 (2 <sup>nd</sup> ¶), page 93 through page 95, and original Claims 1, 7, 141, 142 and 168. The specification also provides support for detecting the nucleic acids by means of fluorescent dyes, including fluorescein, rhodamine and dansyl. <i>See, e.g.</i> , page 26, 1 <sup>st</sup> ¶; example 9 on pages 46 through 47; page 96, last ¶ through page 97 1 <sup>st</sup> ¶, and original Claims 42, 43, 88, 89, and 130-133.
determining the sequence of said nucleic acid of interest from said detected fragments.	The specification provides support for detecting fragments on a sequencing gel, <i>e.g.</i> , page 84, which necessarily includes determining the sequence of the fragments.